Remarks

Status of Claims

Claims 1 – 39 were original in the application. Claims 2 – 6, 9, 10, 17, 20, 21, 23, 24 and 35 – 40 have been cancelled. Claims 1, 7, 8, 12, 18, 19, 25 - 33, and 41 – 50 have been amended. Therefore, claims 1, 7, 8, 11 – 16, 18, 19, 22, 25 – 34 and 41 – 51 are submitted for examination on the merits.

The Drawings

At the suggestion of the Examiner a petition for submission of color drawings in compliance with 37 CFR 1.84 has been submitted with the required fee and drawing copies.

Claim Rejections - 35 *USC§ 112*

Claims 8 and 19 have been amended to provide antecedent basis.

Claim Rejections - 35 *USC§ 102b*

Claims 1, 7, 11-14, 18, 22, 25-29, 31-33, 40-46 and 48 were rejected as being anticipated by **Strid** US Patent No. 5,386,012.

The blood and vascular environment are completely different than the muscle or tendon environment as found in **Strid** in their anatomical, biological and tissue engineering aspects than in the environment of an intravascular thrombus as in the invention. The invention manipulates an intravascular

thrombus to generate clot maturation into scar tissue and aneurysm healing. The invention is also set in the context of the biomechanical forces of blood flow at the level of the neck of the aneurysm, which are the dynamic forces which need to be controlled in order to generate clot maturation and aneurysm healing unlike **Strid**. At the same time the invention must be of such a nature that catastrophic clinical complications are avoided such as thrombosis in situ with occlusion of the parent artery and severe cerebral stroke produced by embolic migration of the clot into the arteries in the brain, which are not faced by **Strid**. All these factors which are material in context of the present invention are totally ignored by **Strid**.

The delivery and manufacturing of the bioactive materials faced in the invention are also totally different and also carry different challenges than in **Strid**. **Strid** incorporates GHK-Cu2 with the idea stimulating new formation of blood vessels and increasing nourishment to the tissue area to be "healed". On the contrary in the context of the invention we want to occlude a blood vessel by clot maturation and transformation into collagen and scar tissue in a vascular aneurysm. This transformation has never been previously tested in contact with flowing blood and in a clot environment.

In regard to claim 1, the Examiner contended that **Strid** discloses an apparatus with a polymeric material able to induce controlled inflammation to form scar tissue in a body cavity to substantially completely occlude the body cavity with out excessive formation of scar tissue, as recited in column 2 and claim 8.

First, claim 8 of **Strid** states:

"8. The implant material of claim 4 wherein said polymer is a copolymer of poly-L-lactic acid and polyglycolic acid."

There is no teaching in claim 8 about scar tissue or occlusion of any body cavity.

Second, col. 2 of **Strid** states in pertinent part:

> ". . . In orthopedic surgery, implants are used for soft parts **such as muscles, tendons and ligaments**. In the case of ligaments, the preferred material used has been polypropylene bands which are unfortunately not degradable, and results have been unfavorable in the long run. When degradable material is used to replace ligaments, it is of utmost importance that this material is biocompatible. Polymers of lactic acid and glycolic acid are degraded to nontoxic products that living tissues tolerate. In the human body they are hydrolyzed to their monomers. . . . "
>
> "Polymers of lactic and glycolic acid have been used for long time as resorbable suture material. When this material is used for artificial ligaments the main problem is that *they hydrolyse so rapidly that the body is not allowed enough time to replace them with its own tissue where collagen constitutes the main part*. The rapid hydrolysis could be compensated for if one could increase the rate of collagen synthesis. "
>
> "The solution: The invention presented here is that the material used for implants incorporates GHK--Cu^2 the copper-complex of the tripeptide glycyl-L-histidyl-L-lysine."

Strid's teaching is in the context of orthopedic surgery and is not applicable to implants used in the vascular system where the tissues being mediated are blood and vascular aneurysms. The physiology of muscles, tendons and ligaments can be expected to very different from that of brain aneurysms. A cavity in which there is a pulsing flow of blood is a very different biological and physical environment than where a ligament finds itself. The existence of complex blood chemistry alone introduces substantial biophysical distinctions. ***Strid** does not disclose how to control the formation of scar tissue in a brain or vascular aneurysm to occlude it.* As a measure of what one with skill

in the art would understand, one can be very sure that the FDA would not approve of the use of the **Strid** implant in a brain aneurysm based on the teaching in **Strid** or consider it as preexisting technology for brain or vascular aneurysms.

There is no teaching in **Strid** which guarantees or even suggests that the solution to aneurysm occlusion in the brain is the use of GHK--Cu^2 bound to a polymer on an implant.

The Examiner also cites **Strid** for disclosing an implant with a copolymer of poly-L-lactic acid and polyglycolic acid, which the Examiner contends would necessarily induce controlled inflammation to induce controlled formation of scar tissue in a body cavity to substantially completely occlude the body cavity with out excessive formation of scar tissue given the structure.

Strid discloses that when poly-L-lactic acid and polyglycolic acid is used for artificial ligaments they hydrolyse so rapidly that collagenous scar tissue is not formed. There is every reason to believe that **Strid** is correct that poly-L-lactic acid and polyglycolic acid does not induce formation of scar tissue in any effective amount, which is exactly the opposite to what the Examiner contends. In other words, in the environment of a ligament there is no inherent formation of scar tissue in any effective amount. If there were, then **Strid's** invention of using GHK--Cu^2 bound to poly-L-lactic acid and polyglycolic acid would not have been necessary.

In regard to claims 7 and 18, the Examiner contends that **Strid** discloses a biocompatible and bioabsorbable polymeric material that is at least one

copolymer that is poly-L-lactic acid and polyglycolic acid as related in claim 8.

Again there is no disclosure whatsoever in the specification of **Strid** regarding the use of a copolymer that is poly-L-lactic acid and polyglycolic acid. Claim 8 is unsupported by any disclosure. Whatever can be gleaned from **Strid** regarding the use of a copolymer of poly-L-lactic acid and polyglycolic acid is in any case limited to orthopedic implants, which as shown above has no inherent applicability to the different application of vascular body cavities.

Nothing is taught in **Strid** in regard to the class of copolymers selected from the group consisting of poly-glycolic acid/poly-L-lactic acid copolymers, polycaprolactive, polyhydroxybutyrate/hydroxyvalerate copolymers, poly-L-lactide, and polydioxanone. **Strid** is silent as to the utility of this class in any kind of implant. Arguendo, disclosure of one element of the class does not disclose the class.

Claim 11 depends on claim 1 and is allowable therewith.

In regard to method claim 12 in the same manner as asserted with respect to claim 1, the Examiner contends that **Strid** discloses a method of causing substantially complete occlusion of a body cavity by inducing the controlled formation of scar tissue in the body cavity without excessive formation of scar tissue.

As demonstrated above **Strid** does not disclose a method of occluding a vascular aneurysm. In fact **Strid** does not disclose a method of occluding a ligament, even if it could understood what occlusion of a ligament might mean. **Strid** is directed to a method of replacing a degrading polymer ligament implant

with collagen. **Strid** is silent not only with respect to vascular aneurysms, with respect to occlusions, but also with respect to avoidance of excessive formation of scar tissue or controlled inflammation. Insofar as the teaching of **Strid** is concerned the collagen even formed in the polymer ligament implant could be excessive and uncontrolled. **Strid** does not address any issues concerning excess or control of the collagen formed.

The Examiner incorrectly asserts that an implant occludes the vascular aneurysm by merely occupying some undefined amount of space without more. Moreover, the issue is irrelevant in that claim 12 does not necessarily claim occlusion.

Claims 13 -14 depend on claim 12 and is allowable therewith.

Claim 22 depends on claim 1 and is allowable therewith.

In regard to claims 25 (an apparatus claim), 41 and 42 (both method claims), the Examiner contends that **Strid** discloses a biocompatible and bioabsorbable polymeric material that has a controlled degradation time (claim 25) to thereby control intravascular inflammatory reactions, degrades faster than implanted metal coils (claim 41), and provides a stronger inflammatory reaction than metal coils (claim 42).

Strid is in fact totally silent as to any control of the degradation of the implant. **Strid** is in fact totally silent as to how polymer implant degradation compares to the degradation of metal coils in the body. **Strid** is in fact totally silent as to how the strength of the collagen inducing GHK--Cu^2 compares to the strength of the collagen inducing metal coils. **Strid** only states that metal

implants can be protein coated if desired. Nothing in **Strid** discloses that if he were to apply his ligament polymer to vascular aneurysms that it would necessarily provide a stronger inflammatory reaction than a metal coil. To contend that **Strid** has any such disclosure is to fabricate content which is not in **Strid** by incorporating the teaching and claims of applicants.

Relative definition of degradation rates and strengths of reactions of a polymer to the same by comparison to the same for metal coils, which is the prior art implant in vascular aneurysm, is definite and clear. Reference to a known standard, such a length compared to a known ruler, is the only definite way that relative quantification of a measure can be clearly understood.

Claims 26 and 43 are dependent on claims 25 and 12 respectively and are allowable therewith. **Strid** teaches immunologic cell interaction in the context of a ligament and not a vascular aneurysm.

Claims 27 and 44 are dependent on claims 25 and 12 respectively and are allowable therewith. **Strid** teaches fibrosis in the context of a ligament and not a vascular aneurysm.

In regard to claims 28 and 45, the Examiner contends that **Strid** discloses a polymer that accelerates fibrosis within an aneurysm to more strongly anchor the implant than does metal coils.

The applicant has not positively recited in the claims that this invention is used in an aneurysm. **Strid** is silent in regard to aneurysms and to any comparison of any measure relative to metal coils in any biological environment. **Strid** is silent in regard to any issue of anchoring anything.

In regard to claims 29 and 46, the Examiner contends that **Strid** discloses a polymer for generating more connective tissue and a less unorganized clot than metal coils so that an occluded aneurysm in which the implant is disposed is more resistant to a water hammer effect of pulsatile blood than when treated by metal coils.

Strid is utterly silent in regard to occlusion of any kind let alone the relative proportions of connective tissue to unorganized clot in a vascular occlusion. Even more so in regard to the relative proportions of connective tissue to unorganized clot, which would render the occluded aneurysm more resistant to the water hammer effect of pulsatile blood than when treated by metal coils.

Again, comparison of a measure of strength or resistance to a certain effect with metal coils is clear and the easiest way by which such relative measures can be understood. The structural feature is the strength of the polymer's inflammatory power as measured by the relative proportion of connective tissue to unorganized clot caused thereby, which is conceptually akin to measuring a weight of a claimed object by how much it extends a spring.

The applicant has positively recited an aneurysm. The scope of the claim is clear.

In regard to claims 31 and 48, the Examiner contends that **Strid** discloses a polymer that would necessarily restrict aneurysm recanalization by accelerated scar formation when used in treating blood vessels.

Again the applicants respectfully maintain that what **Strid** discloses in the case of a ligament does not necessarily compel any conclusion relative to what

would happen in a vascular aneurysm let alone a structure which would be effective to any necessary restriction on recanalization in an aneurysm. **Strid** actually teaches that poly-L-lactic acid and polyglycolic acid degrade faster than collagen can be formed and it is unknown what in fact the tripeptide GHK--Cu^{+2} complex would be effective to do in the environment of a vascular aneurysm. No one would be so foolish as to presently suggest its use in a brain aneurysm based on **Strid's** disclosure. The reaction could be so severe that a tumor would result, or so weak that aneurysm would not be occluded and rupture risked.

Further, applicant has positively recited an aneurysm. Thus, the scope of the claim is clear.

In regard to claim 32, the Examiner contends that **Strid** discloses that a polymer that would necessarily induce organized connective tissue to fill an aneurysm and to retract the aneurysm over time due to maturation of collagen fibers to reduce aneurysm size and decrease aneurysm compression on brain parenchyma or cranial nerves when used in treating blood vessels.

Strid is utterly silent as to identifying any polymer that would necessarily induce organized connective tissue to fill an aneurysm and to retract the aneurysm over time due to maturation of collagen fibers to reduce aneurysm size and decrease aneurysm compression on brain parenchyma or cranial nerves when used in treating blood vessels. Use of a polymer for ligament replacement does not necessarily compel any conclusion whatsoever in regard to what the polymer would or would not achieve in a brain aneurysm.

Functional language does hold patentable weight in apparatus claims

where it serves to limit or define the claimed polymer which is an element of the apparatus, 35 USC 112.

In regard to claim 33, the Examiner contends that **Strid** discloses a polymer that is less thrombogenic than metal coils and would accelerate aneurysm healing with less thrombogenicity.

Strid is totally silent in regard to any polymer that is less thrombogenic than metal coils and would accelerate aneurysm healing with less thrombogenicity than metal coils. The thrombogenicity of metal coils is never discussed in any sense in **Strid**.

Comparison with a known standard or measure like metal coils in an aneurysm to quantify the degree of thrombogenicity is clear.

Rejection Pursuant to 35 USC 103(a)

Claims 8,15,16,19,30,34,47, and 49-51 were rejected as obvious over **Strid**.

Claims 8 and 19 depend on claims 7 and 18 respectively and are allowable therewith. Further, there is no cited or suggested basis by which the selection of fibrinogen, fibronectin, vitronectin, and laminin in a vascular aneurysm for purposes of occlusion could be made.

Claims 15 and 16 depend on claim 14 and are allowable therewith. Further, there is no cited or suggested basis by which the selection of endothelial and basic fibroblast growth factor in a vascular aneurysm for purposes of occlusion could be made.

In regard to claims 30 and 47, the Examiner cites **Strid** as disclosing a coil as an implant, but does not contend that use of a polymer to restrict compaction of the coil by accelerated scar formation is in any suggested.

In regard to claims 49 and 50, the Examiner contends that it would be obvious to employ the implant of **Strid** in an aneurysm for treatments of aneurysms.

No justification or basis is cited for asserting this rather astonishing conjecture. The implantation of ligament implants into brain aneurysms would be almost certain to kill all the patients. At the very least there is a very open question of whether the **Strid** methodology could be adapted to vascular implants to be effective for occlusion. It is just as likely that vascular tumors would be produced or no occlusion would result. It cannot be determined *a priori* which would be the case from **Strid's** disclosure.

In regard to claims 34 and 51, the Examiner contends that **Strid** it would be an obvious design choice select the molar ratio of 90/10 of glycolic to L-lactic acid to control the degree of inflammatory response.

Strid fails to provide any motivation or suggestion that there is any advantage for any purpose to mix polymers or to control the molar ratio of mixed polymers, let alone to control the degree of inflammatory response by using a molar ratio of 90/10. The degree of inflammatory response is a balance between not providing sufficient cellular manipulation to occlude the vascular cavity or providing too much such that a deleterious tumor is formed. The optimal choice of a molar ratio of 90/10 of glycolic to L-lactic acid to control the degree of

inflammatory response comes only from hard developmental work and there was utterly no direction in the prior art as to what formulation would succeed in vascular aneurysms. No direction is provided by **Strid** on this score and no basis is cited by the Examiner to support the bare assertion of design choice.

Advancement of the claims as amended to allowance is respectfully requested.

Respectfully submitted,
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